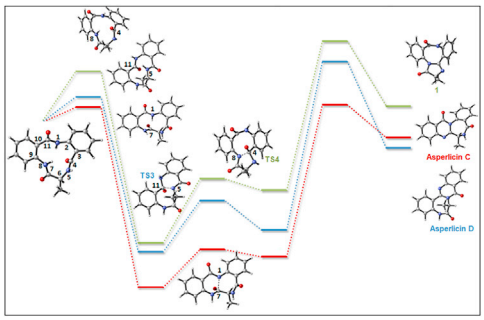
Chemistry & Biology

In This Issue

O-Acetylation of the Microcystins

PAGE 861

Microcystins are a chemically diverse family of cyclic peptide toxins produced by cyanobacteria. Fewer et al. show that the production of *O*-acetylated microcystins is catalyzed by an *O*-acetyltransferase, McyL. Interestingly, McyL belongs to a family of enzymes that inactivate antibiotics through *O*-acetylation.



Making of the Asperlicins

PAGE 870

Asperlicins are alkaloid natural products produced from a fungus. Gao et al. analyzed the function of a nonribosomal peptide synthase involved in asperlicins biosynthesis, AspA, and show that it functions in iterative fashion to transform simple building blocks into the complex structures seen in asperlicins.

Tandem Oxygenations of Manumycin-type Metabolites

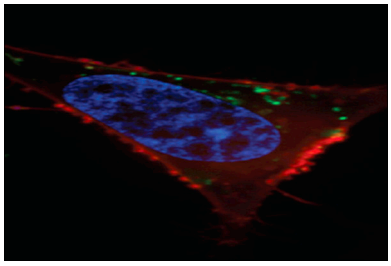
PAGE 879

Epoxyquinone moiety is crucial for various biological functions in number of natural products. Rui et al. reveal a unique mechanism of tandem oxygenations underlying the biosynthesis of epoxyquinone moiety in manumycin metabolites and provide evidence for epoxyquinone moiety's critical role in the anti-MRSA activity.

Proapoptotic Activity of PUMA

PAGE 888

PUMA is a BCL-2 family protein that mediates a host of apoptotic responses. Edwards et al. show that the PUMA death domain, in the form of hydrocarbon-stapled PUMA BH3 helices, directly engages BAX to initiate its functional activation. Thus, PUMA BH3 is a dual antiapoptotic inhibitor and proapoptotic activator.



Quorum Sensing under Proteomic Interrogation

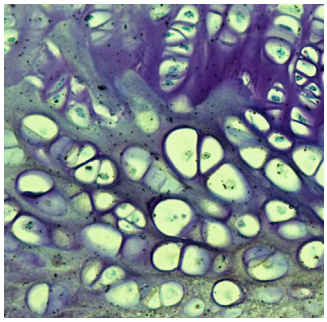
PAGE 903

Lowery et al. use an inhibitor of bacterial communication to monitor changes in the proteome of a pathogen with the aim of discovering new processes regulated by AI-2-based quorum sensing (QS). The QS antagonists are valuable tools to confirm proposed and to elucidate previously unidentified QS pathways.

PIKfyve is a Toll-like Receptor Signaling Player, Says Apilimod

PAGE 912

Apilimod is a small molecular inhibitor of IL-12/23 production. Cai et al. show that PIKfyve is the molecular and therapeutic target of apilimod. Apilimod is a potent yet selective PIKfyve kinase inhibitor. Pharmacological and genetic studies demonstrate PIKfyve is required for TLR-induced production of IL12/23.



Aging and the Cartilage

PAGE 922

Aging takes a toll on all. Scharf et al. use redox proteomic analysis and MS/MS mapping to demonstrate several oxidative posttranslational modifications in structural proteins of intervertebral discs and to determine how protein modifications contribute to one common aspect of aging: cartilage degeneration.

mRNA Display Selection of an FK506-Binding Protein

PAGE 935

Tokunaga et al. identify spartin as an FK506-binding protein. FK506 inhibits interaction of spartin with lipid droplets-associated protein, TIP47; blocks localization of spartin and its binder, an E3 ubiquitin ligase, AIP4, in lipid droplets; and increases protein level of ADRP, a regulator of lipid homeostasis.

Multiple Agents May be Needed for Full CFTR Correction

PAGE 943

VX-809 is a small molecule that rescues function of the major cystic fibrosis-causing mutation F508del CFTR, currently in clinical trial. Farinha et al. assess the additivity and synergy of VX-809 with other rescuing strategies and provide support for the requirement of combined therapies to fully rescue F508del-CFTR.

Resources: From Stem Cells to Alzheimer's Drugs

PAGE 956

Preclinical models for Alzheimer's and other neurodegenerative diseases are in critical demand. McIntire et al. describe a mouse embryonic stem cell-derived neuronal model that recapitulates physiological properties of AD neuron population, bridging the gap between in vitro screening and translational drug discovery.